

Abstract:

Memory loss is a central symptom in different diseases, and represents a significant social and economic burden for a large percentage of European citizens. The molecular and neurobiological bases of memory deficits are largely unknown and there are currently no drugs available that can markedly decelerate or prevent memory decline. To address this major problem, this project will investigate the role of novel synaptic cell adhesion molecules (CAMs) in memory loss, and the therapeutic value of targeting these CAMs to restore memory function and associated neurobiological mechanisms at the synaptic level. The selection of novel synaptic CAMs is based on (1) recent evidence showing that they can recruit the synaptic machinery and form synapses, (2) the implication of CAMs, in general, in synaptic plasticity and memory, and (3) a direct link established between synaptic remodelling and memory formation. We have assembled a multidisciplinary consortium including excellent European researchers in this field, covering a wide range of structural, biochemical, electrophysiological and behavioural expertise. To understand memory loss, three domains have been selected as among the most prominent and widespread disease domains affecting memory and quality of life in our society: psychiatric disorders, the neurodegenerative disorder of Alzheimer's disease, stress and aging. For each disease domain, specific and validated animal models will be used to investigate memory loss on molecular, subcellular, cellular and functional levels. Our approach will result in the preclinical development and validation of mimetic peptides for novel synaptic CAMs as potential drug candidates to treat memory deficits or prevent memory decline. The current proposal offers the groundbreaking possibility to raise the bar in memory research by targeting novel molecules and developing effective drugs to treat memory disturbances based on their biological mechanism.